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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/986,174	11/07/2001	Nabil Hanna	P 0280732 2000-30-0261VUS	4956

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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/986,174	HANNA, NABIL	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16 and 23-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16 and 23-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/19/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 28-36 are new. Claims 16, and 23-36 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

The rejection of claim 25 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the engineered antibody fragment whose sequence has been published, does not reasonably provide enablement for the specifically recited antibodies is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103, Withdrawn

The rejection of claims 16, 17, and 23-28 under 35 U.S.C. 103(a) as being unpatentable over Davis et al., July 2000, Clinical Cancer Research, vol. 6, pages 2644-2652 in view of Taji et al., Jpn. J. Cancer Res., July 1998, vol. 89, pages 748-756 is **withdraw** in view of the amendment to claim 16, along with applicant's persuasive argument.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 25, 33, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The specification as originally filed at page 3 line 8 discloses anti-BI antibody as same as disclosed in Liu et al., J. Clin. Oncol. 16:3270-8. Liu et al., at the abstract, which is "idodine-131-anti-CD20 antibody". The new limitation "tositumomab" includes an un-labeled antibody, and the Office is unable to find support that the claimed invention includes the unlabeled tositummab.

Claims 29-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples,

6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 16, 17, and 23-27 are drawn to method of treating (claims 29-36) or killing lymphoma B cells using an immunoconjugate comprising an anti-CD20 antibody or an immunogenic fragment thereof fused at its carboxy terminus to IFN-alpha-2a.

The specification at page 31, Example 3 discloses dose of 1 microgram to 10 mg of the claimed immunoconjugate is administered, which is 10,000-fold difference. The specification does not teach any other in vivo dose. One of skill in the art would have difficulty accepting that an effective dose would ranges from 1 microgram to 10 mg, where the maximum difference could be 10,000-fold. Applicant during the traversal of the obviousness rejection of even "enhancing apoptosis", mere 1600-fold difference (as compared to 10,000-fold range) would pose problem for one that practice B cell lymphoma treatment method. The amended claims and the newly presented claims are now all drawn to in vivo treatment method.

Davis et al., of record, July 2000, Clinical Cancer Research, vol. 6, pages 2644-2652 represent the state of art for the claimed invention. It was used a reference that the previously presented claims were obvious. Davis teaches at the abstract that combination therapy with rituximab and IFN-alpha-2a in 38 patients with relapsed or refractory, low-grade or follicular, B-cell NHL was effective, wherein the combination therapy was IFN-alpha-2a [2.5 or 5 million units (MIU)] administered s.c., three times weekly for 12 weeks with the mean total units received were 141 MIU (maximum, 180

MIU). As for rituximab, which was started on the fifth week of treatment, rituximab was administered by i.v. infusion (375 mg/m2) weekly for 4 doses.

As applicant correctly calculated at pages 10 and 11 of the Remark's section of the amendment filed on 10/19/2006, the number of molecules of IFN-alpha-2a being administered is 1,600 fold less than the anti-CD20 antibody in the clinical studies of Davis. As applicant pointed in the Remark section, this suggests that if one of skill in the art would follow the effective dose of Davis with the fusion protein of the antibody linked to the interferon, then one of skill has to administer 1,600-fold higher molecule of the interferon. It is not clear what the dosages of the claimed immunoconjugate would be in order to be effective to treat B cell lymphoma: The specification does not provide an adequate guidance on this matter

Considering the unpredictable state of art, limited guidance, no examples in the specification how to use the instantly claimed invention, broad breath of the claims, it is concluded that undue experimentation is required to practice the invention.

Double Patenting

Claim 35 is objected to under 37 CFR 1.75 as being a duplicate of claim 33.

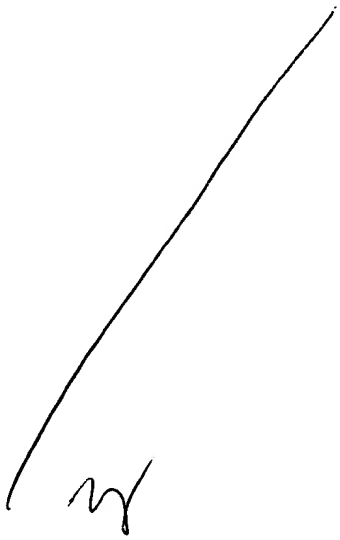
Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MISOOK YU, Ph.D.
Primary Examiner
Art Unit 1642